

Tamoxifen: Questions and Answers

1. What is tamoxifen?

Tamoxifen (Nolvadex[®]) is a medication in pill form that interferes with the activity of estrogen (a hormone). Tamoxifen has been used for more than 20 years to treat patients with advanced breast cancer. It is used as adjuvant, or additional, therapy following primary treatment for early stage breast cancer. In women at high risk of developing breast cancer, tamoxifen reduces the chance of developing the disease. Tamoxifen continues to be studied for the prevention of breast cancer. It is also being studied in the treatment of several other types of cancer. It is important to note that tamoxifen is also used to treat men with breast cancer.

2. How does tamoxifen work on breast cancer?

Estrogen promotes the growth of breast cancer cells. Tamoxifen works against the effects of estrogen on these cells. It is often called an “anti-estrogen.” As a treatment for breast cancer, the drug slows or stops the growth of cancer cells that are present in the body. As adjuvant therapy, tamoxifen helps prevent the original breast cancer from returning and also helps prevent the development of new cancers in the other breast.

3. Are there other beneficial effects of tamoxifen?

While tamoxifen acts *against* the effects of estrogen in breast tissue, it acts *like* estrogen in other tissue. This means that women who take tamoxifen may derive many of the beneficial effects of menopausal estrogen replacement therapy, such as lower blood cholesterol and slower bone loss (osteoporosis).

4. Can tamoxifen prevent breast cancer?

Research has shown that when tamoxifen is used as adjuvant therapy for early stage breast cancer, it reduces the risk of recurrence of the original cancer and also reduces the risk of developing new cancers in the other breast. Based on these findings, the National Cancer Institute (NCI) funded a large research study to determine the usefulness of tamoxifen in preventing breast cancer in women who have an increased risk of



developing the disease. This study, known as the Breast Cancer Prevention Trial (BCPT), was conducted by the National Surgical Adjuvant Breast and Bowel Project (NSABP), a component of the NCI's Clinical Trials Cooperative Group Program. This study found a 49 percent reduction in diagnoses of invasive breast cancer among women who took tamoxifen. Women who took tamoxifen also had 50 percent fewer diagnoses of noninvasive breast tumors, such as ductal or lobular carcinoma in situ. However, there are risks associated with tamoxifen. Some are even life threatening. The decision to take tamoxifen is an individual one: The woman and her doctor must carefully consider the benefits and risks of therapy.

Women with an increased risk of developing breast cancer have the option to consider taking tamoxifen to reduce their chance of developing this disease. They may also consider participating in the Study of Tamoxifen and Raloxifene (see question 5).

At this time, there is no evidence that tamoxifen is beneficial for women who do not have an increased risk of developing breast cancer.

5. What is the Study of Tamoxifen and Raloxifene (STAR), and how can a woman learn more about it?

The Study of Tamoxifen and Raloxifene (STAR) is a clinical trial (a research study conducted with people) designed to see whether the osteoporosis drug raloxifene (Evista[®]) is more or less effective than tamoxifen in reducing the chance of developing breast cancer in women who are at an increased risk of developing the disease. Raloxifene may have breast cancer risk reduction properties similar to those found in tamoxifen. This study will also examine whether raloxifene has benefits over tamoxifen, such as fewer side effects.

The STAR trial, which began in June 1999, is being conducted by the NSABP. It will involve about 22,000 postmenopausal women who are at least 35 years old and are at increased risk for developing breast cancer.

Women can learn more about the STAR trial in several ways. They can call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). The number for deaf and hard of hearing callers with TTY equipment is 1-800-332-8615. Information is also available on NSABP's Web site at <http://www.nsabp.pitt.edu> or on the Study of Tamoxifen and Raloxifene (STAR) Trial Digest Page on the NCI's Web site at <http://cancer.gov/star> on the Internet.

6. What are some of the more common side effects of taking tamoxifen?

In general, the side effects of tamoxifen are similar to some of the symptoms of menopause. The most common side effects are hot flashes and vaginal discharge. Some women experience irregular menstrual periods, headaches, fatigue, nausea and/or vomiting, vaginal dryness or itching, irritation of the skin around the vagina, and skin rash. As is the case with menopause, not all women who take tamoxifen have these

symptoms. Men who take tamoxifen may experience headaches, nausea and/or vomiting, skin rash, impotence, or a decrease in sexual interest.

7. Does tamoxifen cause cancers of the uterus?

Tamoxifen increases the risk of two types of cancer that can develop in the uterus: endometrial cancer, which arises in the lining of the uterus, and uterine sarcoma, which arises in the muscular wall of the uterus. Like all cancers, endometrial cancer and uterine sarcoma are potentially life-threatening. Women who have had a hysterectomy (surgery to remove the uterus) and are taking tamoxifen are not at increased risk for these cancers.

Endometrial cancer

In the BCPT, women who took tamoxifen had more than twice the chance of developing endometrial cancer compared with women who took a placebo (an inactive substance that looks the same as, and is administered in the same way as, tamoxifen). The risk of endometrial cancer in women taking tamoxifen was in the same range as (or less than) the risk in postmenopausal women taking single-agent estrogen replacement therapy. This risk is about 2 cases of endometrial cancer per 1,000 women taking tamoxifen each year.

Most of the endometrial cancers that have occurred in women taking tamoxifen have been found in the early stages, and treatment has usually been effective. However, for some breast cancer patients who developed endometrial cancer while taking tamoxifen, the disease was life threatening.

Uterine sarcoma

Information collected by the U.S. Food and Drug Administration indicates that women who have used tamoxifen for breast cancer treatment or prevention have an increased risk of developing uterine sarcoma. Review of all the NSABP clinical trials using tamoxifen confirmed an increased risk of this rare cancer. In the BCPT, there are about 2 cases per 10,000 women taking tamoxifen each year. Research to date indicates that uterine sarcomas are more likely to be diagnosed at later stages than endometrial cancers, and may therefore be harder to control and more life-threatening than endometrial cancer.

Abnormal vaginal bleeding and lower abdominal (pelvic) pain are symptoms of cancers of the uterus. Women who are taking tamoxifen should talk with their doctor about having regular pelvic examinations, and should be checked promptly if they have any abnormal vaginal bleeding or pelvic pain between scheduled exams.

8. Does tamoxifen cause blood clots or stroke?

Data from large treatment studies suggest that there is a small increase in the number of blood clots in women taking tamoxifen, particularly in women who are receiving anticancer drugs (chemotherapy) along with tamoxifen. The total number of women who

have experienced this side effect is small. The risk of having a blood clot due to tamoxifen is similar to the risk of a blood clot when taking estrogen replacement therapy.

Women in the BCPT who took tamoxifen also had an increased chance of developing blood clots and an increased chance of stroke.

9. Does tamoxifen cause eye problems?

As women age, they are more likely to develop cataracts (a clouding of the lens inside the eye). Women taking tamoxifen appear to be at increased risk for developing cataracts. Other eye problems, such as corneal scarring or retinal changes, have been reported in a few patients.

10. Does tamoxifen cause other types of cancer?

Although tamoxifen can cause liver cancer in particular strains of rats, it is not known to cause liver cancer in humans. It is clear, however, that tamoxifen can sometimes cause other liver toxicities in patients, which can be severe or life threatening. Doctors may order blood tests from time to time to check liver function.

One study suggested a possible increase in cancers of the digestive tract among women receiving tamoxifen for breast cancer. Other trials, including the BCPT, have not shown an association between tamoxifen and these cancers.

Studies such as the BCPT show no increase in cancers other than uterine cancer. This potential risk is being evaluated.

11. Should women taking tamoxifen avoid pregnancy?

Yes. Tamoxifen may make premenopausal women more fertile, but doctors advise women on tamoxifen to avoid pregnancy because animal studies have suggested that the use of tamoxifen in pregnancy can cause fetal harm. Women who have questions about fertility, birth control, or pregnancy should discuss their concerns with their doctor.

12. Does tamoxifen cause a woman to begin menopause?

Tamoxifen does not cause a woman to begin menopause, although it can cause some symptoms that are similar to those that may occur during menopause. In most premenopausal women taking tamoxifen, the ovaries continue to act normally and produce estrogen in the same or slightly increased amounts.

13. Do the benefits of tamoxifen in treating breast cancer outweigh its risks?

The benefits of tamoxifen as a treatment for breast cancer are firmly established and far outweigh the potential risks. Patients who are concerned about the risks and benefits of

tamoxifen or any other medications are encouraged to discuss these concerns with their doctor.

14. How long should a patient take tamoxifen for the treatment of breast cancer?

Patients with advanced breast cancer may take tamoxifen for varying lengths of time, depending on their response to this treatment and other factors. When used as adjuvant therapy for early stage breast cancer, tamoxifen is generally prescribed for 5 years. However, the ideal length of treatment with tamoxifen is not known.

Two studies have confirmed the benefit of taking adjuvant tamoxifen daily for 5 years. These studies compared 5 years of treatment with tamoxifen with 10 years of treatment. When taken for 5 years, the drug reduces the risk of recurrence of the original breast cancer and also reduces the risk of developing a second primary cancer in the other breast. Taking tamoxifen for longer than 5 years is not more effective than 5 years of therapy.

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Sources of National Cancer Institute Information

Cancer Information Service

Toll-free: 1-800-4-CANCER (1-800-422-6237)

TTY (for deaf and hard of hearing callers): 1-800-332-8615

NCI Online

Internet

Use <http://cancer.gov> to reach the NCI's Web site.

LiveHelp

Cancer Information Specialists offer online assistance through the *LiveHelp* link on the NCI's Web site.

This fact sheet was reviewed on 5/13/02